

**AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-19 (cancelled)

Claim 20 (currently amended): A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of a vaccine comprising a ~~free-living microbe~~modified bacterium, wherein the nucleic acid of the ~~microbe~~bacterium has been modified by reaction with a nucleic acid targeted compound that reacts directly with the nucleic acid so that the ~~microbe~~modified bacterium is attenuated for proliferation relative to the bacterium prior to modification, wherein gene expression in the modified bacterium is active.

Claim 21 (currently amended): A method of inducing an immune response in a host to an antigen comprising administering to the host an effective amount of a vaccine comprising a ~~free-living microbe~~modified bacterium, wherein the nucleic acid of the ~~microbe~~bacterium has been modified by reaction with a nucleic acid targeted compound that reacts directly with the nucleic acid so that the ~~microbe~~modified bacterium is attenuated for proliferation relative to the bacterium prior to modification, and wherein the ~~microbe~~modified bacterium expresses the antigen.

Claims 22-82 (cancelled)

Claim 83 (previously presented): The method of claim 20, wherein the nucleic-acid targeted compound is a nucleic acid alkylator.

Claim 84 (previously presented): The method of claim 83, wherein the nucleic acid alkylator is  $\beta$ -alanine, N-(acridin-9-yl), 2-[bis(2-chloroethyl)amino]ethyl ester.

Claim 85 (previously presented): The method of claim 20, wherein the nucleic acid targeted compound is activated by irradiation.

Claim 86 (previously presented): The method of claim 85, wherein the nucleic acid targeted compound is a psoralen compound activated by UVA irradiation.

Claim 87 (previously presented): The method of claim 86, wherein the nucleic acid targeted compound is 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen.

Claims 88-96 (cancelled)

Claim 97 (currently amended): The method of claim 9620, wherein the bacterium comprises a genetic mutation that attenuates the ability of the ~~microbe~~bacterium to repair its nucleic acid that has been modified relative to wild type.

Claim 98 (currently amended): The method of claim 97, wherein the bacterium is defective with respect to a DNA repair enzyme relative to wild type due to the genetic mutation.

Claim 99 (previously presented): The method of claim 98, wherein the genetic mutation is in one or more gene selected from the group consisting of *phrB*, *uvrA*, *uvrB*, *uvrC*, *uvrD* and *recA*.

Claim 100 (currently amended): The method of claim 9620, wherein the ~~microbe~~bacterium is *Mycobacterium tuberculosis*.

Claim 101 (currently amended): The method of claim 9620, wherein the ~~microbe~~bacterium is *Bacillus anthracis*.

Claim 102 (currently amended): The method of claim 9620, wherein the ~~microbe~~bacterium is *Listeria monocytogenes*.

Claim 103 (currently amended): The method of claim 102, wherein the *Listeria* comprises a genetic mutation that attenuates the ability of the ~~microbe~~bacterium to repair its modified nucleic acid ~~that has been modified~~ relative to wild type.

Claim 104 (currently amended): The method of claim 103, wherein the *Listeria* is defective with respect to a DNA repair enzyme relative to wild type due to the genetic mutation.

Claim 105 (previously presented): The method of claim 104, wherein the genetic mutation is in one or more gene selected from the group consisting of *phrB*, *uvrA*, *uvrB*, *uvrC*, *uvrD* and *recA*.

Claim 106 (currently amended): The method of claim 105, wherein the ~~*Listeria* comprises a mutation~~genetic mutation is in one or more gene selected from the group consisting of *uvrA*, *uvrB*, and *uvrC*.

Claim 107 (currently amended): The method of claim 106, wherein the genetic mutation *Listeria* comprises at least one mutation in both *uvrA* and *uvrB*.

Claim 108 (withdrawn – currently amended): The method of claim 107, wherein the *Listeria* further comprises a mutation in the *actA* gene, the *inlB* gene, or both genes, wherein the mutation in the *actA* gene attenuates the ability of the *Listeria* to spread relative to wild type and the mutation in the *inlB* gene attenuates the ability of the *Listeria* to invade at least some cells relative to wild type.

Claim 109 (currently amended): The method of claim 20, wherein the ~~microbe~~bacterium comprises a heterologous nucleic acid sequence encoding an antigen.

Claim 110 (previously presented): The method of claim 20, wherein the vaccine further comprises a pharmaceutically acceptable carrier or an adjuvant.

Claim 111 (currently amended): The method of claim 20, wherein the ~~microbial~~bacterial gene expression of the ~~microbe~~bacterium is substantially unaffected by the modification of the nucleic acid of the bacterium.

Claim 112 (previously presented): The method of claim 20, wherein the disease is an infectious disease.

Claim 113 (previously presented): The method of claim 109, wherein the disease is cancer.

Claim 114 (previously presented): The method of claim 21, wherein the nucleic-acid targeted compound is a nucleic acid alkylator.

Claim 115 (previously presented): The method of claim 114, wherein the nucleic acid alkylator is  $\beta$ -alanine, N-(acridin-9-yl), 2-[bis(2-chloroethyl)amino]ethyl ester.

Claim 116 (previously presented): The method of claim 21, wherein the nucleic acid targeted compound is activated by irradiation.

Claim 117 (previously presented): The method of claim 116, wherein the nucleic acid targeted compound is a psoralen compound activated by UVA irradiation.

Claim 118 (previously presented): The method of claim 117, wherein the nucleic acid targeted compound is 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen.

Claim 119-127 (cancelled)

Claim 128 (currently amended): The method of claim ~~127~~21, wherein the bacterium comprises a genetic mutation that attenuates the ability of the ~~microbe~~bacterium to repair its modifiednucleic acid ~~that has been modified~~ relative to wild type.

Claim 129 (currently amended): The method of claim 128, wherein the bacterium is defective with respect to a DNA repair enzyme relative to wild type due to the genetic mutation.

Claim 130 (previously presented): The method of claim 129, wherein the genetic mutation is in one or more gene selected from the group consisting of *phrB*, *uvrA*, *uvrB*, *uvrC*, *uvrD* and *recA*.

Claim 131 (currently amended): The method of claim ~~127~~21, wherein the ~~microbe~~bacterium is *Mycobacterium tuberculosis*.

Claim 132 (currently amended): The method of claim ~~127~~21, wherein the ~~microbe~~bacterium is *Bacillus anthracis*.

Claim 133 (currently amended): The method of claim ~~127~~21, wherein the ~~microbe~~bacterium is *Listeria monocytogenes*.

Claim 134 (currently amended): The method of claim 133, wherein the *Listeria* comprises a genetic mutation that attenuates the ability of the ~~microbe~~bacterium to repair its nucleic acid that has been modified relative to wild type.

Claim 135 (currently amended): The method of claim 134, wherein the *Listeria* is defective with respect to a DNA repair enzyme relative to wild type due to the genetic mutation.

Claim 136 (previously presented): The method of claim 135, wherein the genetic mutation is in one or more gene selected from the group consisting of *phrB*, *uvrA*, *uvrB*, *uvrC*, *uvrD* and *recA*.

Claim 137 (currently amended): The method of claim 136, wherein the genetic mutation is *Listeria* ~~comprises a mutation~~ in one or more gene selected from the group consisting of *uvrA*, *uvrB*, and *uvrC*.

Claim 138 (currently amended): The method of claim 137, wherein the genetic mutation *Listeria* comprises at least one mutation in both *uvrA* and *uvrB*.

Claim 139 (withdrawn - currently amended): The method of claim 138, wherein the *Listeria* further comprises a mutation in the *actA* gene, the *inlB* gene, or both genes, wherein the mutation in the *actA* gene attenuates the ability of the *Listeria* to spread relative to wild type and the mutation in the *inlB* gene attenuates the ability of the *Listeria* to invade at least some cells relative to wild type.

Claim 140 (currently amended): The method of claim 21, wherein the ~~microbe~~bacterium comprises a heterologous nucleic acid sequence encoding the antigen.

Claim 141 (previously presented): The method of claim 21, wherein the vaccine further comprises a pharmaceutically acceptable carrier or an adjuvant.

Claim 142 (currently amended): The method of claim 21, wherein the ~~microbial~~bacterial gene expression of the ~~microbe~~bacterium is substantially unaffected by the modification of the nucleic acid of the bacterium.

Claim 143 (previously presented): The method of claim 140, wherein the antigen is a tumor antigen.

Claim 144 (previously presented): The method of claim 143, wherein the tumor antigen is mesothelin, SPAS-1, proteinase-3, SP-17, gp100, PAGE-4, TARP, Her-2/neu, WT-1, NY-ESO-1, PSMA, K-ras or CEA, or an antigen derived from mesothelin, SPAS-1, proteinase-3, SP-17, gp100, PAGE-4, TARP, Her-2/neu, WT-1, NY-ESO-1, PSMA, K-ras or CEA.

Claim 145 (previously presented): The method of claim 140, wherein the antigen is an infectious disease antigen.

Claim 146 (previously presented): The method of claim 145, wherein the antigen is derived from a Human Immunodeficiency Virus or a hepatitis virus.

Claim 147 (previously presented): The method of claim 146, wherein the antigen is derived from hepatitis C virus.

Claim 148 (currently amended): The method of claim ~~12721~~12721, wherein the bacterium is *Salmonella* or *Shigella*.

Claim 149 (currently amended): The method of claim ~~9620~~9620, wherein the bacterium is *Salmonella* or *Shigella*.